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EXAMINER	
DUFFY, BRADLEY	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,450	PETERS ET AL.	
	Examiner	Art Unit	
	BRADLEY DUFFY	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,18-20 and 23-27* is/are pending in the application.

4a) Of the above claim(s) *10,11 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,18-20,23,24,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed May 26, 2009, is acknowledged and has been entered. Claims 1, 18-20, 23 and 25 have been amended. Claims 12-17 and 21-22 have been canceled. Claims 26 and 27 have been newly added.

2. Claims 1-11, 18-20 and 23-27 are pending in the application.

3. Claims 10-11 and 25 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant elected without traverse in the reply filed October 14, 2008.

4. Claims 1-9, 18-20 and 23, 24, 26 and 27 are under examination. As detailed in the previous office action the species of retinoid under examination are all-*trans* retinoic acid, 9-*cis* retinoic acid, and retinoic acid.

Response to Amendment

5. The amendment filed on May 26, 2009, is considered non-compliant because it fails to meet the requirements of 37 CFR § 1.121, as amended on June 30, 2003 (see *68 Fed. Reg. 38611*, Jun. 30, 2003). However, in order to advance prosecution, rather than mailing a Notice of Non-Compliant Amendment, Applicant is advised to correct the following deficiencies in replying to this Office action:

The amendment to the claims is non-compliant because it presents the incorrect status identifier for claim 25. Notably, this claim was withdrawn in the previous office action and the amendment does not identify the claim as withdrawn as required by 37 CFR § 1.121.

Applicant is reminded: Only the corrected section(s) of the non-compliant amendment must be resubmitted (in its entirety), e.g., the entire "Amendments to the claims" section of applicant's amendment must be re-submitted. 37 CFR § 1.121(h).

Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, Applicant's amendment and/or arguments filed May 26, 2009, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed December 26, 2008.

Grounds of Objection Maintained

Oath/Declaration

7. The objection to the declaration is maintained.

In the reply filed May 26, 2009, Applicant submits that a new declaration has been provided.

While the new declaration is acknowledged, it is also defective because it does not indicate that there any additional declaration pages attached e.g., to page 2 of the oath, i.e., the pages do not indicate that they are page 1 of 3, page 2 of 3 or page 3 of 3, respectively.

Accordingly a new oath or declaration in compliance with 37 CFR 1.63 including the entire inventive entity is required. See MPEP 201.03, 605.04 and 37 CFR 1.63.

In order to correct this issue it is suggested that the pages of the new oath recite page 1 of 3, page 2 of 3 and page 3 of 3, respectively.

Specification

8. The disclosure is objected to because of the following informalities:

The objection to the specification because, in the first sentence, the status of Application 10/778,915 needs to be updated to indicate that it is now abandoned, is maintained.

The specification amendment filed May 26, 2009, did not update the status and Applicant's response did not otherwise address this objection.

Appropriate correction is required.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. The rejection of claims 1-9, 18-20 and 23, 24, 26 and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained.

Claims 1-9, 18-20 and 23, 24, 26 and 27 are indefinite because claim 1 recites an immunoglobulin that exhibits a serum half-life of 15-20 days after administration to said patient, said serum half-life being determined by enzyme linked immunosorbent assay (ELISA).

At page 9 of the amendment filed May 26, 2009, Applicant has submitted that the rejection has been addressed by the amendment to claim 1.

In response, the amendment has not obviated the rejection for the following reasons:

In this case, while the claims have been amended to recite that the immunoglobulin exhibits a serum half life of 15-20 after administration to said patient and that the half-life is determined by ELISA, the claims remain indefinite because as explained in the previous office action, the half-life will vary greatly depending on the conditions of the assay system used and these differences would still occur even if the determination was by ELISA because different ELISA assays could be used and the half-life could be measured in different patients under different conditions. Notably, using different ELISA assays the specification also identifies different half-lives for the immunoglobulin at page 19, which depend on the period of time the half-life is measured over, as set forth in the previous office action. Additionally, at page 20 the specification also identifies 3 more different serum half-lives using different ELISA assays. Accordingly, it is apparent that depending of the ELISA assay used widely different serum half-life values would be obtained. Once again, since the ELISA assay

conditions can vary such that different serum half-life values would be obtained depending on the particular conditions, the metes and bounds of the claims would vary depending on the conditions used; accordingly, these claims fail to delineate the metes and bounds of the subject matter that Applicant regards as the invention with the requisite particularity and clarity to permit the skilled artisan to know or determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

Accordingly, after careful and complete consideration of Applicant's amendment, it is maintained that these claims fail to delineate the metes and bounds of the subject matter that Applicant regards as the invention with the requisite clarity and particularity to permit the skilled artisan to know or determine infringing subject matter.

In this case, the Examiner suggests obviating the rejection by amending the claims to remove reference to serum half-lives.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. The rejection of claims 1-9, 18-20 and 23, 24, 26 and 27 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "written description" rejection.

At page 9 of the amendment filed May 26, 2009, Applicant has submitted that the amendments to the claims have obviated this ground of rejection.

Again, the considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published

Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

In this case, as they have been amended, the claims are broadly drawn to methods of treating a diverse subgenus of "**malignant** tumorous diseases", which may or may not express an elevated level of the human EpCAM antigen relative to corresponding healthy tissue, in a human patient which comprise administering a diverse genus of human "immunoglobulins" comprising the amino acid sequences of SEQ ID NO:1 and 2 that specifically bind to the human EpCAM antigen.

Accordingly, as a first point, the amendment has not obviated the rejection because as set forth in the previous office action "the genus of immunoglobulins encompasses a structurally and functionally diverse genus of proteins that includes antibodies, T-cell antigen receptors, MHC molecules and other antibody-like molecules (Elgert et al. Immunology: Understanding the Immune System, 1996, page 59, of record). Furthermore, Elgert defines immunoglobulins, "as a family of globular proteins that comprise antibody molecules and molecules having patterns of molecular structure (antigenic determinants) in common with antibodies," and that "immunoglobulin can be used to refer to any antibody-like molecule". However, in this case, the specification only adequately describes a human antibody comprising a heavy chain with the amino acid sequence of SEQ ID NO:1 and a light chain amino acid sequence of SEQ ID NO:2" that specifically binds to the human EpCAM antigen (see e.g., page 17-19). While antibodies are a subgenus of the "immunoglobulin" genus, the written description in this case only describes with the requisite particularity required human "antibodies" comprising a heavy chain with the amino acid sequence of SEQ ID NO:1 and a light chain amino acid sequence of SEQ ID NO:2 that bind human EpCAM antigen because the specification does not describe immunoglobulins, such as T-cell antigen receptors, MHC molecules and other antibody-like molecules which comprise a heavy chain with the amino acid sequence of SEQ ID NO:1 and a light chain amino acid sequence of SEQ ID NO:2 and antibodies comprising a heavy chain with the amino acid sequence of

SEQ ID NO:1 and a light chain amino acid sequence of SEQ ID NO:2 would not be considered representative of T-cell antigen receptors, MHC molecules and other antibody-like molecules which comprise a heavy chain with the amino acid sequence of SEQ ID NO:1 and a light chain amino acid sequence of SEQ ID NO:2 due to the structural differences in these molecules.

Secondly, while the claims have been amended to be drawn to a subgenus of "malignant tumorous diseases", it is noted that the specification teaches that it is only expected that "the method of the invention may be efficaciously applied to any disease in which EpCAM expression is elevated in the disease state relative to the healthy state of a given tissue" at page 25. Accordingly, it is submitted that one of skill in the art would not recognize that Applicant was in possession of the claimed methods as amended to recite "malignant tumorous diseases" because one of skill in the art could not immediately envision, recognize or predict whether the recited methods would treat malignant tumorous diseases that do not show elevated or any expression of human EpCAM antigen.

Accordingly, after careful and complete consideration of Applicant's amendments and response, for these reasons, the specification as filed does not adequately describe the methods to which the claims are directed and this rejection is maintained.

13. The rejection of claims 1-9, 18-20 and 23, 24, 26 and 27 under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for using** methods encompassed by the claims that are taught by the prior art, **does not reasonably provide enablement for using** the claimed processes, including, for example, the claimed process for treating *any* malignant tumorous disease by administering *any* human "immunoglobulin" comprising the amino acid sequences of SEQ ID NO:1 and 2, is maintained. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

MPEP § 2164.01 states:

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

At page 9 of the amendment filed May 26, 2009, Applicant has submitted that the amendments to the claims have obviated this ground of rejection.

In response, the amendment has not obviated the rejection for the following reasons:

In this case, as they have been amended, the claims are broadly drawn to methods of treating a diverse subgenus of "**malignant** tumorous diseases", which may or may not express an elevated level of the human EpCAM antigen relative to corresponding healthy tissue, in a human patient which comprise administering a diverse genus of human "immunoglobulins" comprising the amino acid sequences of SEQ ID NO:1 and 2 that specifically bind to the human EpCAM antigen.

As explained in the above rejection of the claims, as failing to satisfy the written description requirement, because the claims are now directed to processes of using a genus of human "immunoglobulins" comprising the amino acid sequences of SEQ ID NO:1 and 2 that specifically bind to the human EpCAM antigen that have not been described so as to permit the skilled artisan to immediately envision, recognize or distinguish the members of these genera, the skilled artisan could not make these "human immunoglobulins" without undue and/or unreasonable experimentation; and if these "human immunoglobulins" cannot be made without undue and/or unreasonable experimentation, the specification would not reasonably enable the skilled artisan to use the claimed processes without undue experimentation. Notably, e.g., one of skill in the art would be subject to undue experimentation to make the claimed immunoglobulins,

such as T-cell antigen receptors, MHC molecules and other antibody-like molecules which comprise the amino acid sequences of SEQ ID NO:1 and 2 and which specifically bind to the human EpCAM antigen because the specification contains, no specific non-general guidance as to how to make such human EpCAM "immunoglobulins".

Secondly, in light of the amendment to recite methods of treating a subgenus of "malignant tumorous diseases", it is noted that specification does not present specific, non-general guidance that would allow one of skill in the art to treat such a subgenus of cancers by the recited methods because such a subgenus encompasses cancers which do not express human EpCAM antigen and cancers that express human EpCAM antigen at levels similar to corresponding healthy tissue. Notably, at page 25, the specification sets forth that is expected that the methods of the invention may be applied when human EpCAM expression is elevated compared to expression in healthy tissue, so it is submitted that one of skill in the art would be subject to undue experimentation to use the recited methods to treat the malignant tumorous diseases reasonably commensurate with the full scope of such diseases.

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Thus, the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify other processes of treating malignant tumorous diseases that are encompassed by the claims.

In conclusion, upon careful and full consideration of Applicant's amendments and response and the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enabled the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation, and this rejection is being maintained.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

16. The rejection of claims 1-9, 18-20 and 23, 24, 26 and 27 under 35 U.S.C. 103(a) as being unpatentable over Kufer et al (WO 98/46645 A2, 1998, of record), in view of Raum et al (Can. Immunol. Immunother., 50:141-150, 2001, of record) and Naundorf et al (Int. J. Can. 100:101-110, 2002, of record) and as evidenced by Oberneder et al (Eur. J. Can., 42:2530-2538, 2006, of record), Loh et al (J. Nuc. Med., 39:484-489, 1998, of record) and Leyland-Jones (J. Clin. Onc., 221(21):3965-3971, 2003, of record), is maintained.

Starting at page 10 of the amendment filed May 26, 2009, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

In this traversal, Applicant appears to argue that while the amino acid sequences SEQ ID NO:1 and SEQ ID NO:2 correspond to the MT201 antibody sequences of the prior art, the prior art fails to teach or suggest a specific regimen of administering the antibody no more frequently than once every two weeks. Applicant further comments that this regimen corresponds to approximately the half-life of the antibody and ensures that the total serum concentration of the antibody never drops below the minimum level necessary for continued efficacy and that the Examiner's argument that it would have been obvious to one ordinarily skilled in the art to have determined the most appropriate doses, schedules and routes of administration for an antibody therapy, is both unsupported and untrue.

In response, as a first point, Applicant's argument is not found persuasive with respect to the prior art not teaching and/or suggesting administering the antibody no more frequently than once every two weeks. Notably, Kufer et al teach methods of administering the MT201 antibody, which as explained in the previous office action is referred to by the designation H79 in Kufer, to humans at a suitable dose (see entire document, e.g., abstract and pages 1, 2 12 and 17). Nowhere does Kufer et al teach that the administration must occur *more* frequently than once every two weeks. Therefore, the teachings of Kufer clearly encompass methods of administration such as a single dose administration to patients, and such methods are encompassed by the step of administering no more frequently than once every two weeks. Furthermore, it is noted that Kufer et al also teach that administering a murine monoclonal antibody that targets the human EpCAM antigen present on minimal residual colorectal cancer once a month for 4 months for a total of 5 doses improved 5 year mortality rates by 30% compared to untreated patients (see e.g., page 2[1]). Accordingly, it is submitted that the

[1] See reference C10 from IDS filed 5/29/07 which evidences that the antibody was administered once a month

prior art does teach and/or suggest administering the antibody no more frequently than once every two weeks to treat colon cancer.

Secondly, with the respect to the Examiner's argument that it would have been obvious to one ordinarily skilled in the art to have determined the most appropriate doses, schedules and routes of administration for the antibody therapy, the argument was supported with the following evidence and scientific reasoning.

Notably, as set forth in the previous office action, it is a common objective in the art to establish a dose, schedule, and route of delivery that is both safe and effective, so as achieve optimal therapeutic effect and maximal benefit. See *In re Boesch*, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." (citations omitted)). See *In re Peterson*, 65 USPQ2d 1379 1382 (CA FC 2003): "The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages." In this case, the prior art of Kufer et al and Raum et al both teach that the human MT201 antibody was cytotoxic to human colon cancer, and additionally that the antibody had advantageous properties such as longer serum half-life, improved cytotoxic effector functions and immunogenicity as compared to a murine antibody that binds the human EpCAM antigen which can treat colon cancer patients, so one of skill in the art would have clearly recognized that the MT201 antibody would treat colon cancer and that it was a result effective variable that could be used in art known methods of treating colon cancer patients expressing the human EpCAM antigen. Therefore, one of skill in the art clearly would have been motivated to establish a dose, schedule, and route of delivery that is both safe and effective, so as achieve optimal therapeutic effect and maximal benefit for the MT201 antibody in treating colon cancer patients.

Furthermore, the motivation to do so was further evidenced by Loh et al (J. Nuc. Med., 39:484-489, 1998, of record) (see entire document) and Leyland-Jones (J. Clin. Onc., 221(21):3965-3971, 2003, of record) (see entire document) in the previous office action, who both evidence that the pharmacokinetic analysis and pharmacokinetic

simulations used to establish a dose, schedule, and route of delivery for therapeutic antibodies are known, routine and in conventional use in the art. Accordingly, it is unclear on what basis or evidence Applicant is submitting that the Examiner's argument is unsupported and untrue. Once again, it is submitted that once a therapeutic antibody which can treat colon cancer was identified, such as the instantly recited antibody that was known in the prior art, that one of skill in the art would be motivated to establish a dose, schedule, and route of delivery that is both safe and effective, so as achieve optimal therapeutic effect and maximal benefit in order to establish that the antibody can be used clinically.

Finally, as set forth in the previous office action, this position is also reasonable since parameters such as dosing, scheduling and routes of delivery, which are used to treat any given cancer or patient, may be expected to differ from those that are used most effectively to treat another cancer or patient. In general, these parameters that are used most efficaciously can only be determined in clinical trials designed to determine those parameters. The Office, however, does not have the facilities or resources for conducting clinical trials to determine if therapeutic agents are used effectively in particular regimens, as in accordance with the claims; so, in the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed process is different than that taught and/or suggested by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989). In this case, while the claims have been limited to a particular antibody at a schedule no more than once every two weeks, the claims otherwise encompass a broad range of malignant tumors, doses, schedules and parameters and as explained above, the prior art teaches the same antibody and teaches and/or suggests administering the antibody no more frequently than once every two weeks.

Thus, it would have been obvious to one ordinarily skilled in the art at the time the invention was made to have determined the most appropriate doses, schedules, and routes of administration, so as to practice the disclosed process of treating colon

cancer as effectively as possible. One ordinarily skilled in the art at the time the invention was made to do so to optimize the effectiveness of the treatment.

Once again, one of skill in the art would have been motivated to do so and would have had a reasonable expectation of success at arriving at methods as encompassed by the instant claims, since the antibody was known in the prior art to be cytotoxic to human colon cancer cells, methods of treating colon cancer patients with antibodies that bind the human EpCAM antigen as encompassed by the claims were known and/or suggested in the prior art and the pharmacokinetic analysis and pharmacokinetic simulations needed to establish a dose, schedule, and route of delivery that is both safe and effective, so as achieve optimal therapeutic effect and maximal benefit in order for the antibody to be used clinically were routine and conventional in the prior art.

Therefore, the claimed methods as a whole were obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Accordingly, after careful and complete consideration of Applicant's response, for these reasons and the reasons of record as explained in the preceding Office action, this rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

17. Claims 26-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a NEW MATTER rejection.

In this case, new claims 26 and 27 recite that the human immunoglobulins comprise a heavy chain with the amino acid sequence of SEQ ID NO:1 a light chain with the amino acid sequence of SEQ ID NO:2 and exhibit a serum half-life of 15, 16, 17, 18, 19 or 20 days.

Applicant has not indicated where support occurs in the specification for these newly added limitations.

Notably, M.P.E.P. § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims". See M.P.E.P. § 714.02 and § 2163.06.

Nevertheless, as M.P.E.P. § 2163 further states: "The examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the original disclosure a description of the invention defined by the claims. See *Wertheim*, 541 F.2d at 263, 191 USPQ at 97".

After reviewing the specification, it does not appear that the specification, including the claims, as originally filed, provides adequate support for the language of the amended claims. In this case, although the specification sets forth at page 19, that the human antibody comprising a heavy chain with the amino acid sequence of SEQ ID NO:1 and a light chain with the amino acid sequence of SEQ ID NO:2 can have an observed serum half-life measured in one assay as 14.74+/- 4.23 days, which would appear to support the range of 15-20 days recited in claim 1, support for a human antibody comprising a heavy chain with the amino acid sequence of SEQ ID NO:1 and a light chain with the amino acid sequence of SEQ ID NO:2 having half-lives of exactly 15, 16, 17, 18, 19 or 20 days could not be found in the specification as filed.

Notably, since the specification teaches that the half-life of this antibody is variable, it is submitted that new claims which recite that the half-life of this antibody is exactly 15, 16, 17, 18, 19 or 20 days has in fact introduced new concepts, thereby violating the written description requirement set forth under 35 U.S.C. §112, first paragraph.

Otherwise this issue might be resolved if Applicant were to point to other disclosures in the specification, including the claims, as originally filed, which are believed to provide the necessary written support for the language of the instant claims.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Roovers et al (Can. Immunol. Immunther., 50:51-59, 2001, of record) teach human antibodies which bind to human EpCAM antigen that bind to colon cancer cells. Wolf et al (DDT., 7(5):S25-S27, 2002) teach that the MT201 antibody has a half-life of several weeks in primates.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,
Brad Duffy
571-272-9935

/Stephen L. Rawlings/
Primary Examiner, Art Unit 1643

/bd/
Examiner, Art Unit 1643
July 9, 2009